

Version with markings to show changes made

In the Specification:

At page 7, the section entitled "Brief Description of the Drawings" has been deleted.

At page 19, the first paragraph has been amended as follows:

The uptake experiments were carried out in Dulbecco medium, in the presence and absence of added fatty acid-free BSA (BSA) or fatty acid-loaded BSA (BSA/FA). The results of studies of the uptake of ^{125}I -BBI, either as the native-BBI or in conjugated form to palmitic or oleic acid, in Caco-2 cells in the presence of serum-free medium [are presented in Fig. 1. The results are shown] were determined as the average ng of BBI internalized \pm SEM, $n=3$. The uptake of ^{125}I -BBIssPal into the cells was approximately 100-fold higher than that of ^{125}I -BBI. Similarly, the uptake of ^{125}I -BBIssOleic into the cells was about 108-fold higher than ^{125}I -BBI. The difference between the uptake of ^{125}I -BBIssPal and ^{125}I -BBIssOleic were not significant.

The paragraph bridging pages 19 and 20 has been amended as follows:

The results of the biodistribution of BBI and BBIssPal following iv-administration [are shown in Fig. 2] were determined as the % dose accumulated per g organ \pm SEM. The results indicated that while BBI was rapidly excreted from the body without attaining high

results indicated that while BBI was rapidly excreted from the body without attaining high blood levels, BBIssPal was accumulated in the blood at a relatively high level and was apparently more slowly removed [form] from the circulation. The kidney biodistribution results indicated that while BBI was rapidly accumulated in the kidneys, BBIssPal was not. The liver accumulation of BBIssPal was approximately 5-fold higher than that of BBI, and BBIssPal levels remained high in the liver even at 24 hr post-injection. The lung accumulation of BBIssPal was also approximately 2-fold higher than that of BBI, but this result may have been caused by the residual blood present in the organ after its excision. Clearly, BBIssPal was retained longer and at a higher level in the blood and the liver. On the other hand, the kidney clearance of BBIssPal was about 4-fold lower than native-BBI.

At page 20, the first full paragraph has been amended as follows:

The iv-biodistribution of BBI and BBIssOleic were also studied in CF-1 mice. The results [are presented in Fig. 3] were determined as the % dose accumulated per g of the organ \pm SEM, n=3, at 0.5, 3 and 24 hr. The biodistribution of BBIssOleic was very similar to BBIssPal. As was observed for BBIssPal, BBIssOleic had higher blood levels than BBI and was apparently more slowly cleared from the circulation. The blood levels of BBIssOleic were about 4-fold higher than those of BBI at the same time points. The kidney clearance of BBIssOleic was approximately 4-fold lower, and the liver accumulation approximately 4-fold higher than native-BBI. The retention of BBIssOleic in the liver was prolonged, with significant levels of the conjugate present in the liver even at 24 hr post-injection. The lung

levels of BBIssOleic were about 2-fold higher than native-BBI levels, but the higher residual blood in the lungs could account for this observation.

The paragraph bridging pages 20 and 21 has been amended as follows:

The ip-biodistribution of ^{125}I -BBIssPal in CF-1 mice [is shown in Fig. 4] was determined as the average % dose accumulation per organ \pm range [(bars)] at 0.5 hr [(Fig. 4A)], 3 hr [(Fig. 4B)] or 24 hr post-injection [(Fig. 4C)]. The kidney accumulation of ^{125}I -BBIssPal was 4-fold lower than that of native ^{125}I -BBI for the 0.5 and 3 hr time points. At 24 hr, ^{125}I -BBIssPal levels were higher in the kidneys than ^{125}I -BBI. The blood level of ^{125}I -BBIssPal was similar to that of ^{125}I -BBI at 0.5 hr, 1.5 -fold higher than BBI at 3 hr, and approximately 3-fold higher than BBI at 24 hr. The liver accumulation of ^{125}I -BBIssPal was 1.5-fold higher than ^{125}I -BBI at 0.5 hr, 2.5-fold higher at 3 hr, and about 4-fold higher at 24 hr. Relatively large amounts of ^{125}I -BBIssPal were present in the liver and the kidneys at 24 hr.

The paragraph bridging pages 24 and 25 has been amended as follows:

BBI was modified with 2 or 4 palmitic acids, and the transport was determined in transwells. The cumulative transport of BBI, BBI modified with 4 palmitic acids [BBIssPal(4)], and BBI modified with 2 palmitic acids [BBIssPal(2)] in Caco-2 monolayers [is shown in Fig. 5A; the results are expressed] were determined as BBI (ng/monolayer) \pm

SEM, n=3. The order of the transport extent was BBIssPal(4)>BBI>BBIssPal(2). The results of the internalization of the conjugates into the same cells [is shown in Fig. 5B] were determined as the ng of BBI internalized per monolayer. As expected, BBIssPal(4) had the highest uptake into the cells, followed by BBIssPal(2) and BBI. The basal media obtained at 24 hr from the transwells was analyzed using a G50 column[; the results are shown in Fig. 6]. As had been observed before, neither BBI nor BBIssPal(4) was transcytosed across the monolayers. However, a small, but significant, amount of the basal media of BBIssPal(2) consisted of intact conjugate. This quantity consisted of between about 10 and about 20% of the total radioactivity present in the basal medium.